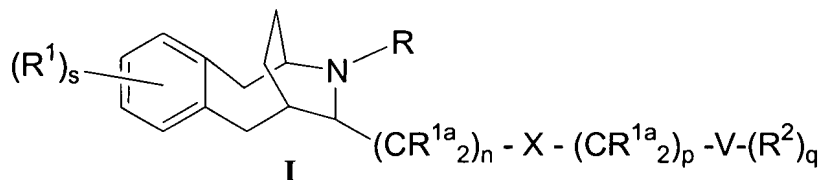


Please amend the claims as shown below:

1. (Currently Amended) A compound of Formula I



wherein

R is selected from

- 1) H,
- 2) ~~OR⁴;~~
- 3) unsubstituted or substituted C<sub>1</sub>-C<sub>10</sub> alkyl,
- 4) unsubstituted or substituted aryl,
- 5) ~~unsubstituted or substituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl,~~
- 6) unsubstituted or substituted heterocycle,
- 7) ~~C(O)R⁴;~~
- 8) ~~C(O)OR⁴, and~~
- 9) ~~C(O)N(R⁴)₂;~~

R<sup>1a</sup> is independently selected from

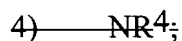
- 1) H,
- 2) unsubstituted or substituted C<sub>1</sub>-C<sub>6</sub> alkyl, and
- 3) OR⁴;

R<sup>1b</sup> is independently selected from

- 1) H, and
- 2) unsubstituted or substituted C<sub>1</sub>-C<sub>6</sub> alkyl;

X is selected from

- 1) a bond,
- 2) C(O), and
- 3) O, and



R<sup>1</sup> is independently selected from

- 1) H,
- 2) halo,
- 3) OR<sup>4</sup>,
- 4) NO<sub>2</sub>,
- 5) —S(O)<sub>m</sub>R<sup>4</sup>;
- 6) —CN
- 7) unsubstituted or substituted C<sub>1</sub>-C<sub>10</sub> alkyl,
- 8) —unsubstituted or substituted aryl;
- 9) —unsubstituted or substituted C<sub>2</sub>-C<sub>6</sub> alkenyl;
- 10) —unsubstituted or substituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl;
- 11) —unsubstituted or substituted alkynyl;
- 12) —unsubstituted or substituted heterocycle;
- 13) —C(O)R<sup>4</sup>,
- 14) C(O)OR<sup>4</sup>,
- 15) C(O)N(R<sup>4</sup>)<sub>2</sub>,
- 16) —S(O)<sub>m</sub>N(R<sup>4</sup>)<sub>2</sub>; and
- 17) N(R<sup>4</sup>)<sub>2</sub>;

V is selected from aryl and heterocycle;

- 1) —H,
- 2) —CF<sub>3</sub>;
- 3) —aryl;
- 4) —heterocycle; and
- 5) —C<sub>3</sub>-C<sub>10</sub> cycloalkyl;

R<sup>2</sup> is independently selected from

- 1) H,
- 2) unsubstituted or substituted C<sub>1</sub>-C<sub>10</sub> alkyl,
- 3) —(CR<sup>1b</sup>)<sub>t</sub>OR<sup>4</sup>,
- 4) Halo,

- 5) CN,
- 6) NO<sub>2</sub>,
- 7) CF<sub>3</sub>,
- 8)  $-(CR^{1b})_tN(R^4)_2$ ,
- 9)  $-C(O)OR^4$ ,
- 10)  $-C(O)R^4$ ,
- 11)  $-S(O)_2R^4$ ,
- 12)  $-(CR^{1b})_tNR^4(CR^{1b})_tR^5$ ,
- 13)  $-(CR^{1b})_tS(O)_mNR^4$ ,
- 14)  $-C(O)OR^4R^5$ ,
- 15)  $-NR^4C(O)R^4$ ,
- 16) ~~unsubstituted or substituted aryl, and~~
- 17) ~~unsubstituted or substituted heterocycle;~~

R<sup>4</sup> is independently selected from

- 1) H,
- 2) unsubstituted or substituted C<sub>1</sub>-C<sub>10</sub> alkyl,
- 3) unsubstituted or substituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl,
- 4) unsubstituted or substituted aryl,
- 5) unsubstituted or substituted heterocycle, and
- 6) CF<sub>3</sub>;

R<sup>5</sup> is independently selected from

- 1) unsubstituted or substituted aryl, and
- 2) unsubstituted or substituted heterocycle;

m is independently 0, 1 or 2;

n is 0 to ~~6~~ 4;

p is 0 to ~~6~~ 4;

q is 0 to ~~6~~ 4, provided that when V is H or CF<sub>3</sub>, q is 0; and

s is 0 to 16;

t is independently 0 to 6;

or a pharmaceutically acceptable salt or stereoisomer thereof.

2. (Currently Amended) The compound according to Claim 1 wherein R<sup>1b</sup>, R<sup>4</sup>, R<sup>5</sup> and variables m, n, p, q and t are as defined in Claim 1 and

R is selected from

- 1) H,
- 2) ~~OR<sup>4</sup>,~~
- 3) unsubstituted or substituted C<sub>1</sub>-C<sub>10</sub> alkyl, and
- 4) ~~unsubstituted or substituted aryl.~~

R<sup>1a</sup> is independently selected from

- 1) H, and
- 2) unsubstituted or substituted C<sub>1</sub>-C<sub>6</sub> alkyl;

X is selected from

- 1) a bond, and
- 2) C(O);

R<sup>1</sup> is independently selected from

- 1) H,
- 2) halo,
- 3) OR<sup>4</sup>,
- 4) N(R<sup>4</sup>)<sub>2</sub>,
- 5) NO<sub>2</sub>, and
- 6) ~~unsubstituted or substituted C<sub>1</sub>-C<sub>10</sub> alkyl;~~

V is selected from aryl and heterocycle;

- 1) ~~H,~~
- 2) ~~CF<sub>3</sub>,~~
- 3) ~~aryl, and~~
- 4) ~~heterocycle;~~

R<sup>2</sup> is independently selected from

- 1) H,
- 2) unsubstituted or substituted C<sub>1</sub>-C<sub>10</sub> alkyl,
- 3)  $(\text{CR}^{1b})_t\text{OR}^4$ ,
- 4) Halo,
- 5)  $\text{CN}$ ,
- 6)  $\text{NO}_2$ ,
- 7)  $\text{CF}_3$ ,
- 8)  $(\text{CR}^{1b})_t\text{N}(\text{R}^4)_2$ ,
- 9)  $\text{C}(\text{O})\text{OR}^4$ ,
- 10)  $(\text{CR}^{1b})_t\text{S}(\text{O})_m\text{NR}^4$ ,
- 11)  $(\text{CR}^{1b})_t\text{NR}^4(\text{CR}^{1b})_t\text{R}^5$ ,
- 12)  $\text{C}(\text{O})\text{OR}^4\text{R}^5$ , and
- 13)  $\text{NR}^4\text{C}(\text{O})\text{R}^4$ ,

s is 0 to 6;

or a pharmaceutically acceptable salt or stereoisomer thereof.

3. (Currently Amended) The compound according to Claim 1 wherein R<sup>1b</sup>, X, R<sup>1</sup>, R<sup>2</sup>, R<sup>4</sup>, R<sup>5</sup> and variables m and t are as defined above and:

R<sup>1a</sup> is independently selected from

- 1) H, and
- 2) unsubstituted or substituted C<sub>1</sub>-C<sub>6</sub> alkyl;

V is phenyl; ~~selected from~~

- 1) ~~aryl~~, and
- 2) ~~heterocycle~~;

n is 0 or 1; ~~to 3~~;

p is 0 to 3;

q is 0 to 3;

or a pharmaceutically acceptable salt or stereoisomer thereof.

4. (Original) A compound that is:

(6*R*,9*S*,11*R*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [*a*][8]annulene;

(6*R*,9*R*,11*S*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [*a*][8]annulene;

(6*S*,9*R*,11*R*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [*a*][8]annulene;

(6*S*,9*R*,11*S*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [*a*][8]annulene;

(6*S*,9*R*,11*S*)-11-benzyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [*a*][8]annulene;

(6*S*,9*R*,11*R*)-11-benzyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [*a*][8]annulene;

(6*R*,9*S*,11*S*)-11-benzyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [*a*][8]annulene;

(6*R*,9*S*,11*R*)-11-benzyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [*a*][8]annulene;

(6*S*,9*R*,11*S*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)  
benzo[*a*][8]annulene;

(6*S*,9*R*,11*R*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)  
benzo[*a*][8]annulene;

(6*R*,9*S*,11*S*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)  
benzo[*a*][8]annulene;

(6*R*,9*S*,11*R*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)  
benzo[*a*][8]annulene;

(6*S*,9*R*,11*S*)-11-(1,3-benzodioxol-5-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-  
(epiminomethano)benzo[*a*][8]annulene;

(6*S*,9*R*,11*R*)-11-(1,3-benzodioxol-5-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*R*,9*S*,11*S*)-11-(1,3-benzodioxol-5-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*R*,9*S*,11*R*)-11-(1,3-benzodioxol-5-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*S*,9*R*,11*S*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulen-4-amine;

(6*S*,9*R*,11*R*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulen-4-amine;

(6*R*,9*S*,11*S*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulen-4-amine;

(6*R*,9*S*,11*R*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulen-4-amine;

(6*S*,9*R*,11*S*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulen-1-amine;

(6*S*,9*R*,11*R*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulen-1-amine;

(6*R*,9*S*,11*S*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulen-1-amine;

(6*R*,9*S*,11*R*)-11-(3-bromobenzyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulen-1-amine;

(6*S*,9*R*,11*S*)-11-(1-benzofuran-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*S*,9*R*,11*R*)-11-(1-benzofuran-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*R*,9*S*,11*S*)-11-(1-benzofuran-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*R*,9*S*,11*R*)-11-(1-benzofuran-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*S*,9*R*,11*S*)-11-(1,3-oxazol-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*S*,9*R*,11*R*)-11-(1,3-oxazol-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*R*,9*S*,11*S*)-11-(1,3-oxazol-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*R*,9*S*,11*R*)-11-(1,3-oxazol-2-ylmethyl)-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo[*a*][8]annulene;

(6*S*,9*R*,11*S*)-11-isopentyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*S*,9*R*,11*R*)-11-isopentyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*R*,9*S*,11*S*)-11-isopentyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*R*,9*S*,11*R*)-11-isopentyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

or a pharmaceutically acceptable salt or stereoisomer thereof.



5. (Original) A compound according to Claim 4 that is:

(6*R*,9*S*,11*R*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*R*,9*R*,11*S*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*S*,9*R*,11*R*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

(6*S*,9*R*,11*S*)-11-phenyl-5,6,7,8,9,10-hexahydro-6,9-(epiminomethano)benzo [a][8]annulene;

or a pharmaceutically acceptable salt or stereoisomer thereof.

6. (Withdrawn) A pharmaceutical composition which is comprised of a compound in accordance with Claim 1 and a pharmaceutically acceptable carrier.

7. (Withdrawn) A method of modulating the catalytic activity of protein kinases in a mammal in need thereof comprising contacting the protein kinase with a compound of Claim 1.

8. (Withdrawn) The method of Claim 7 wherein the protein kinase is an RTK.

9. (Withdrawn) The method of Claim 8, wherein the RTK is selected from IR, IGF-1R and IRR.

10. (Withdrawn) A method of treating or preventing a PK-related disorder in a mammal in need thereof comprising administering to said mammal a therapeutically effective amount of a compound of Claim 1.

11. (Withdrawn) A method of Claim 10, wherein the PK-related disorder is an IGF-1R-related disorder selected from:

- 1) cancer,
- 2) diabetes,
- 3) an autoimmune disorder,
- 4) a hyperproliferation disorder,

- 5) aging,
- 6) acromegaly, and
- 7) Crohn's disease.

12. (Withdrawn) A method of treating cancer in a mammal in need of such treatment comprising administering to said mammal a therapeutically effective amount of a compound of Claim 1.

13. (Withdrawn) A method of treating retinal vascularization comprising administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Claim 1.

14. (Withdrawn) A method of treating cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a second compound selected from:

- 1) an estrogen receptor modulator,
- 2) an androgen receptor modulator,
- 3) retinoid receptor modulator,
- 4) a cytotoxic agent,
- 5) an antiproliferative agent,
- 6) a prenyl-protein transferase inhibitor,
- 7) an HMG-CoA reductase inhibitor,
- 8) an HIV protease inhibitor,
- 9) a reverse transcriptase inhibitor, and
- 10) an angiogenesis inhibitor.

15. (Withdrawn) The method of Claim 14, wherein the second compound is an estrogen receptor modulator selected from tamoxifen and raloxifene.

16. (Withdrawn) A method of treating cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with radiation therapy.

17. (Withdrawn) The method of Claim 16 wherein radiation therapy is also administered.
18. (Withdrawn) A method of treating cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 and paclitaxel or trastuzumab.
19. (Withdrawn) A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 and a GPIIb/IIIa antagonist.
20. (Withdrawn) The method of Claim 19 wherein the GPIIb/IIIa antagonist is tirofiban.
21. (Withdrawn) A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a COX-2 inhibitor.